

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

APPL. NO. : 10/551,234  
APPLICANT : Université Laval  
TITLE : S100 PROTEIN AS NEUTROPHIL ACTIVATOR FOR  
ALLEVIATING NEUTROPENIA IN CANCER  
TREATMENT  
FILED : July 5, 2006  
ART UNIT : 1646  
EXAMINER : Xiaozhen Xie  
DOCKET NO. : 6013-129US

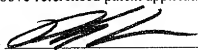
**"KATZ" DECLARATION OF PHILIPPE A. TESSIER**  
**UNDER 37 CFR 1.132**

Sir:

I, Philippe A. Tessier, do hereby solemnly declare that:

1. I am a citizen of Canada and am employed as an associate professor by Laval University in Québec, Canada. A copy of my *c.v.* is enclosed herewith as Exhibit A.
2. I am a co-inventor of US Patent Application serial number 10/551,234 filed on July 5, 2006.
3. The publication by Ryckman *et al.* (2003) emanates from my laboratory and the experiments described therein were carried out under my supervision. The subject matter of this reference therefore originates from me and the other co-inventors named in this patent application (Ryckman, Vandal and Rouleau), and not from another person.
4. The fifth author of the publication by Rickman *et al.* (2003) (i.e. Mariève Talbot) was involved in technical aspects of the research and experiments under my supervision and instructions.
5. I, the undersigned, declare further that all statements made herein of my own knowledge are true; and further that the statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under 18 U.S.C. § 1001 of the United States Code, and that such willful false statements may jeopardize the validity of any patent issued for the above-referenced patent application.

Signed



Dated:

27/05/2008

Philippe A. Tessier

## CURRICULUM VITAE

### PERSONNAL INFORMATION

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**Address:** Home: 1056, de St-Sébastien  
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**Nationality:** Canadian

**Languages:** French, English

## EDUCATION

- 1996-1999: Post-Doctoral Studies, Leukocyte Adhesion Laboratory, Imperial Cancer Research Fund, London, United Kingdom.  
Supervisor: Dr Nancy Hogg
- 1992-1996: Ph.D., Department of Microbiology-Immunology, Faculty of Medicine, Université Laval, Ste-Foy, Québec, Canada.  
Supervisor: Dr Paul H. Naccache, Co-Supervisor: Dr Shaun R. McColl  
Titre de la Thèse: "*Expression et rôle physiologique des molécules d'adhésion et des chimiokines dans l'inflammation synoviale*".
- 01-05/1995: « Visiting Fellow », Department of Microbiology and Immunology, The University of Adelaide, Adelaide, Australia.
- 1994-1995: « School Visitor », Division of Clinical Sciences, The John Curtin School of Medical Research, The Australian National University, Canberra, Australia.
- 1990-1992: M.Sc., Department of Physiology-Endocrinology, Faculty of Medicine, Université Laval, Ste-Foy, Québec, Canada.  
Supervisor: Dr Shaun R. McColl, Co-Supervisor: Dr Marie Audette.  
Titre du mémoire: "*Expression et rôle physiologique de la ICAM-1 dans les fibroblastes synoviaux rhumatoïdes*".
- 1987-1990: B.Sc., Department of Biochemistry, Faculty of Sciences, Université Laval, Ste-Foy, Québec, Canada.

## ACADEMIC POSITION

- 2004-present Associate Professor, Department of Medical Biology, Faculty of Medicine, Université Laval
- 1999-2004 Assistant Professor, Department of Medical Biology, Faculty of Medicine, Université Laval

## OTHER ACTIVITIES

- 2008-present Adjunct Professor, Institut National de la Recherche Scientifique-Institut Armand Frappier
- 2003-present Member, Program committee, Microbiologie-Immunologie, Université Laval
- 2006-2007 Member, Commission des études, Université Laval
- 2005-2007 President, CPE Centre Jour Management Board, Québec, Canada
- 2002-2007 Université Laval's appointee, CPE Centre Jour Management Board, Quebec, Canada
- 2004-2005 Treasurer, CPE Centre Jour, Québec, Canada
- 1997-1998 Scientific writer, Le Matininternet (<http://matin.qc.ca/indexcyra.html>).

## AWARDS

### Scholarship

- 2008-2011 Chercheur-boursier Senior, Fonds de la recherche en Santé du Québec, Canada  
2003-2007 Chercheur-boursier Junior 2, Fonds de la Recherche en Santé du Québec, Canada  
1999-2003 Research Scholar, Arthritis Society of Canada, Canada

### Post-Doctoral studies

- 1997-2000 Fellowship, Medical Research Council of Canada, Canada  
1997-2000 Fellowship, Imperial Cancer Research Fund, United Kingdom  
1997-1999 Fellowship, Arthritis Society of Canada, Canada (declined)  
1996-1998 Fellowship Arthritis Society of Canada / Medical Research Council of Canada, Canada (declined)

### Ph.D.

- 1991-1994 Studentship, Fonds de la Recherche en Santé du Québec, Canada  
1991-1996 Studentship, Arthritis Society of Canada, Canada

## GRANTS

- 2008-2009 **Effect of autotaxin inhibitors with potent antagonistic activity at LPA receptors on collagen-induced arthritis**, \$50 000, Canadian Arthritis Network, Canada, Co-investigator.  
Aim of the study: This grant is aimed at determining the role of autotaxin in a mouse model of arthritis.
- 2007-2012 **Role of S100A8, S100A9, and S100A12 in neutrophil migration to inflammatory sites**, \$125 498, Canadian Institutes of Health Research, Canada, principal investigator.  
Aim of the study: The aim of this grant is to determine the mechanism of action of S100 proteins in directing neutrophil migration to inflammatory sites, with a particular emphasis on inflammatory bowel diseases.
- 2007-2008 **Effects of S100A8 and S100A9 inhibitors on collagen-induced arthritis**, \$50 000, Canadian Arthritis Network, Canada, principal investigator.  
Aim of the study: This grant is aimed at determining the role of S100A8 and S100A9 in a mouse model of arthritis.
- 2005-2010 **The Multi-Cellular Basis of Urate-induced Arthropathies**, US\$222 000/year, National Institutes of Health, U.S.A., co-investigator.  
Aim of the study: This grant is aimed at studying the effect of monosodium urate crystals on leukocytes.
- 2004-2005 **Blockade of S100A8, S100A9, and S100A12 as a new treatment for arthritis**, \$60,000/year, Institute of Musculoskeletal health and arthritis (Canadian Institutes of Health Research), Principal Investigator  
Aim of the study: This grant is aimed at generating blockers of S100A8, S100A9, and S100A12 and at testing these inhibitors as new therapeutic avenues for the treatment of arthritis
- 2003-2006 **Development of a plant based vaccination platform for hepatitis C virus**, \$185 404/year, Natural Sciences and Engineering Research Council, Canada, co-

investigator.

- 2002-2005 **Aim of the study:** This grant is aimed at generating an hepatitis C virus vaccine by modifying the Papaya Mosaic Virus to express hepatitis C virus proteins.  
**Role of S100A8, S100A9, and S100A12 in neutrophil migration to inflammatory sites**, Principal Investigator, \$98,208/year, Canadian Institutes of Health Research, Canada
- 2000-2001 **Aim of this grant:** This grant is aimed at cloning, sequencing and characterising the receptors for S100A8, S100A9, and S100A12.  
**Laboratoire d'étude de la migration des leucocytes**. Co-investigator, \$195,953 (Total budget \$490,294), Canadian Foundation for Innovation, Canada  
Equipment grant for the purchase of an intravital videomicroscope and a confocal microscope.
- 2000-2001 **Starting Fund**, Principal Investigator, \$40,000, Régie Régionale de la Santé et des Services Sociaux, Canada  
Equipment grant
- 1999-2002 **Inflammation in gout : Role of the MRP proteins**, Principal Investigator, \$65,000/year Arthritis Society of Canada, Canada  
**Aim of the study:** This grant was aimed at investigating the involvement of S100A8 and S100A9 in the generation of the inflammatory response associated with gout.
- 1999-2001 **Rôle des protéines MRP dans l'inflammation de la goutte**. Principal Investigator, \$20,000/year, Fonds de la Recherche en Santé du Québec, Canada  
Equipment grant
- 1999-2000 **Persistent Organic Pollutants (POPs) et inflammation**. Co-investigator, \$15,000 for one year, Réseau de recherche en santé environnementale – FRSQ, Canada  
**Aim of the study :** This grant was a pilot study of the effect of the POPs dieldrin and toxaphen on human neutrophil functions.
- 1999 **Subvention de démarrage**, Principal Investigator, \$15,000, Centre de Recherche du CHUL  
Equipment grant

## RESEARCH CONTRACTS

- 2001-2003 **Use of MRPs to induce neutrophilia**. Principal Investigator, \$238,600, Innovatech-Québec, Canada

## PUBLICATIONS

1. N. Anceriz, C. Gilbert, P.A. Tessier. S100A9 enhances neutrophil migration across endothelial cells in response to IL-8 by activating  $\beta 2$  integrins. **Submitted to *J. Leuk Biol.***
2. A. Chakravarti, M.-A. Raquil P.A. Tessier, P.E. Poubelle. RANKL increased at the surface of Toll-like receptor 4-stimulated neutrophils activates osteoclasts and is a receptor for reverse signaling. **Submitted to *J. Exp. Med.***

3. P. Pouliot, I. Plante, M.-A. Raquil, P.A. Tessier, M. Olivier. Myeloid-Related Proteins Rapidly Modulate Macrophage Nitric Oxide Production During Innate Immune Response. **Conditionally accepted in *J. Immunol.***
4. M.-A. Raquil, N. Anceriz, P. Rouleau, P.A. Tessier. 2008. Blockade of antimicrobial proteins S100A8 AND S100A9 inhibits phagocytes migration to the alveoli in streptococcal pneumonia. *J. Immunol.* 180(5):3366-3374.
5. E. Lorenz, M.S. Muhlebach, P.A. Tessier, N.E. Alexis, R. Duncan Hite, M.C. Seeds, D.B. Peden, W. Meredith. 2008. Different expression ratio of S100A8/A9 and S100A12 in acute and chronic lung diseases. *Respir Med*, 102(4):567-73
6. K. Mitchell, H.Y. Yang, P.A. Tessier, W.T. Muhly, W.D. Swaim, I. Szalayova, J.M. Keller, E. Mezey, M.J. Iadarola. 2008. Localization of S100A8 and S100A9 expressing neutrophils to spinal cord during peripheral tissue inflammation. *Pain*, 134(1-2):216-31.
7. F. Kukulski, F. Ben Yebdri, J. Lefebvre, M. Warny, P.A. Tessier, J. Sévigny. 2007. Extracellular nucleotides mediate LPS-induced neutrophil migration in vitro and in vivo. *J. Leuk. Biol.*, 81(5):1269-75.
8. J. Denis, N. Majeau, E. Acosta-Ramirez, C. Savard, M.-C. Bedard, S. Simard, K. Lecours. M. Bolduc, C. Paré, B. Willems, N. Shoukry. P.A. Tessier, P. Lacasse, A. Lamarra, R. Lapointe, C. Lopez Macias. D. Leclerc. 2007. Immunogenicity of papaya mosaic virus like particles fused to a hepatitis c virus epitope: evidence for the critical function of multimerization. *Virology*, 363(1):59-68.
9. N. Anceriz, K. Vandal, P.A. Tessier. 2007. S100A9 mediates neutrophil adhesion to fibronectin through activation of beta2 integrins. *Biochem Biophys Res Commun.* 354(1):84-9.
10. J.N. Jarvis, H.R. Petty, Y. Tang, M.B. Frank, P.A. Tessier, I. Dozmorov, K. Jiang, A. Kindzelski, Y. Chen, C. Cadwell, M. Turner, P. Szodoray, J.L. McGhee, M. Centola. 2006. Evidence for chronic, peripheral activation of neutrophils in polyarticular juvenile rheumatoid arthritis. *Arthritis Res. Ther.* 8(5):R154.
11. K. Greenlee, D.B. Corry, D. Engler, R. Matsunami, P.A. Tessier, R.G. Cook, Z. Werb, F. Kheradmand. 2006. Identification of In Vivo Substrates For MMP2/MMP9 Reveals A Mechanism For Resolution of Inflammation. *J. Immunol.* 177(10):7312-21.
12. A. Hermani, B. De Servi, S. Medunjanin, P.A. Tessier, D. Mayer. 2006. S100A8 and S100A9 activate MAP kinase and NF-kappaB signaling pathways and trigger translocation of RAGE in human prostate cancer cells. *Exp. Cell Res.* 312(2):184-97.
13. S. Bozinovski, M. Cross, R. Vlahos, J.E. Jones, K. Hsu, P.A. Tessier, D.A. Hume, J.A. Hamilton, C.G. Geczy, G.P. Anderson. 2005. Proteomic analysis identifies S100A8 as a glucocorticoid resistant determinant of neutrophilic lung inflammation in vivo. *J. Proteomic Res.* 14(4): 136-145.
14. E. Lorenz, D.C. Chemotti, K. Vandal, P.A. Tessier. 2004. Toll-like receptor 2 represses nonpilus adhesin-induced signaling in acute infections with the *Pseudomonas aeruginosa pilA* mutant. *Infect. Immun.* 72(8): 4561-4569.
15. C. Ryckman, C. Gilbert, R. de Médicis, A. Lussier, K. Vandal, P.A. Tessier. 2004. Monosodium urate monohydrate crystals induce the release of the proinflammatory protein S100A8/A9 from neutrophils. *J. Leukoc. Biol.*, 76(2): 433-440.
16. M. Jaramillo, I. Plante, N. Ouellet, K. Vandal, P.A. Tessier, M. Olivier. 2004. Hemozoin-inducible proinflammatory events in vivo: potential role in malaria infection. *J. Immunol.*, 172(5) :3101-3110.

17. K. Vandal, P. Rouleau, A. Boivin, C. Ryckman, M. Talbot, P.A. Tessier. 2003. Blockade of S100A8 and S100A9 suppresses neutrophil migration in response to LPS. *J. Immunol.* 171(5):2602-2609.
18. C. Ryckman, S.R. McColl, K. Vandal, R. de Médecis, A. Lussier, P.E. Poubelle, P.A. Tessier. 2003. Role of S100A8 and S100A9 in neutrophil recruitment in response to monosodium urate crystals in the air pouch model of acute gouty arthritis. *Arthritis Rheum.* 48(8): 2310-2320.
19. P. Rouleau, K. Vandal, C. Ryckman, P.E. Poubelle, A. Boivin, M. Talbot, P.A. Tessier. 2003. The calcium-binding protein S100A12 induces neutrophil adhesion, migration, and release from bone marrow in mouse at concentrations similar to those found in human inflammatory arthritis. *Clin. Immunol.* 107(1): 46-54.
20. C. Ryckman, K. Vandal, P. Rouleau, M. Talbot, P.A. Tessier. 2003. Proinflammatory activities of S100 proteins: S100A8, S100A9 and S100A8/A9 stimulate neutrophil chemotaxis and adhesion. *J. Immunol.* 170(6):3233-3242.
21. C. Ryckman, G.A. Robichaud, J. Roy, R. Cantin, M.J. Tremblay, P. A. Tessier. 2002. HIV-1 transcription and virus production are both accentuated by the proinflammatory myeloid related proteins in human CD4+ T lymphocytes. *J. Immunol.* 169(6): 3307-3313.
22. M. Robinson, P.A. Tessier, R. Poulson, N. Hogg. 2002. The S100 family heterodimer, MRP-8/14, binds with high affinity to heparin and heparan sulphate glycosaminoglycans on endothelial cells *J. Biol. Chem.* 277(5): 3658-3665
23. M. Pelletier, C. J. Roberge, M. Gauthier, K. Vandal, P.A. Tessier, D. Girard. 2001. Activation of human neutrophils *in vitro* and dieldrin-induced neutrophilic inflammation *in vivo*. *J. Leuk. Biol.*, 70(3): 367-373.
24. R. Henderson, L.H.K. Lim, P.A. Tessier, M. Mathies, M. Perretti and N. Hogg. 2001.The use of LFA-1 deficient mice to determine the role of LFA-1, Mac-1 and  $\alpha 4$  integrin in the inflammatory response of neutrophils. *J. Exp. Med.*, 194(2): 219-226
25. M. Gauthier, C.J. Roberge, M. Pelletier, P.A. Tessier, D. Girard. 2001. Activation of human neutrophils by technical toxaphene. *Clin. Immunol. Immunopathol.*, 98(1):46-53.
26. P.A. Tessier, P.H. Naccache, K.R. Diener, R.P. Gladue, K. Neote, I. Clarke-Lewis, S.R. McColl. 1998. Induction of acute inflammation *in vivo* by Staphylococcal superantigens. II. Critical role for chemokines, ICAM-1, and TNF $\alpha$ . *J. Immunol.*, 161(3): 1204-1211.
27. K.D. Diener, P.A. Tessier, J.D. Fraser, F. Kontgen, S.R. McColl. 1998. Induction of acute inflammation *in vivo* by staphylococcal superantigens I. Leukocyte recruitment occurs independently of T lymphocytes and major histocompatibility complex Class II molecules. *Lab. Invest.*, 78(6): 647-656.
28. P.A. Tessier, K.R. Diener, P.H. Naccache, R.P. Gladue, K. Neote, I. Clarke-Lewis, S.R. McColl. 1997. Chemokine networks *in vivo*: Involvement of both C-X-C and C-C chemokines in neutrophil extravasation in response to tumour necrosis factor  $\alpha$ . *J. Immunol.* 159(7): 3595-3602.
29. P.A. Tessier, P. Cattaruzzi, S.R. McColl. 1996. Inhibition of lymphocyte adhesion to cytokine-activated synovial fibroblasts by glucocorticoids involves the attenuation of vascular cell adhesion molecule 1 and intercellular adhesion molecule 1 gene expression. *Arthritis Rheum.* 39(2): 226-234.
30. P.A. Tessier, M. Audette, P. Cattaruzzi, S.R. McColl. 1993. Upregulation by tumor necrosis factor $\alpha$  of intercellular adhesion molecule-1 expression and function in synovial fibroblasts

- and its inhibition by glucocorticoids. *Arthritis Rheum.* 36(11):1528-39.
31. M. Bouillon, P. Tessier, R. Bouliane, R. Destrempe, M. Audette. 1991. Regulation by retinoic acid of ICAM-1 expression on human tumor cell lines. *Biochem Biophys Acta* 1097(2): 95-102.

#### BOOK CHAPTERS

1. P.A. Tessier, D. Girard. 207. in *Inflammation and neutrophils: A short introduction*. D. Girard Ed. Research Signpost, Kerala, India.
2. N. Anceriz, M.A. Raquil, P.A. Tessier. 2007. The proinflammatory functions of S100A8, S100A9, and S100A12. in *Phenotypic and functional changes of neutrophils activated by recently identified modulators*. D. Girard Ed. Research Signpost, Kerala, India.

#### PATENTS

1. Adjuvant viral particles  
Inventors: D. Leclerc, N. Majeau, P.A. Tessier  
Date of filing: 1 July 2003  
Filing number: 10/609,417
2. Compounds and method for modulating inflammatory reactions  
Inventors : P.A. Tessier, K. Vandal, P. Rouleau C. Ryckman  
Date of filing: 5 July 2002  
Filing number: USA 60/393,520  
International filing date: 20 June 2003  
International filing number: PCT/CA03/00939
3. Neutrophil activators and uses thereof  
Inventors: P.A. Tessier, K. Vandal, P. Rouleau C. Ryckman  
Date of filing: 28 March 2003  
Filing number: USA 60/450,022  
International filing date: 25 March 2004  
International filing number: PCT/CA2004/000451
4. Leukemia inhibitory factors and uses thereof  
Inventors: P.A. Tessier, K. Vandal, P. Rouleau C. Ryckman  
Date of filing: 13 July 2004  
Filing number: USA 60/587,033  
International filing date: 13 July 2005  
International filing number: PCT/CA2005/001089

#### PUBLIC OR INVITED LECTURES



1. From inflammation to cancer: the multiple functions of the alarmins S100A8 and S100A9. McGill University, 14 February 2008.
2. Amplification de la réponse immunitaire par les myeloid-related proteins. CHUM, Montreal, 5 April 2007.
3. Des amplificateurs de la réponse immunitaire : les « Myeloid-related proteins ». UQAM, Montreal, Canada, 4 April 2007.
4. S100A8 et S100A9 et la réponse inflammatoire. 5<sup>ième</sup> meeting of the Centre de recherche en rhumatologie et immunologie, Quebec, Canada, 27 november 2006.
5. S100A8 et S100A9 participent au recrutement des phagocytes dans la pneumonie à streptocoque. 48<sup>th</sup> meeting of the Club de Recherches cliniques du Québec, Lac-à-l'Eau-Claire, Canada, 22 September 2006
6. Les protéines S100 et la migration aux sites infectieux. INRS-IAF, Laval, Canada, January 2006.
7. Le cri d'alarme des neutrophils. Centre de Recherche du CHUL, Ste-Foy, Canada, 16 June 2005.
8. Extracellular activities of S100A8, S100A9, and S100A12. NovoNordisk, Copenhagen, Denmark. 9 February 2004
9. Les protéines S100: de petites protéines aux grands destins. Centre de Recherche du CHUL, Quebec city, Canada. 5 February 2004
10. Les myeloid related proteins et la goutte. INRS/IAF-Santé humaine, Montreal, Canada. 15 February 2000.
11. Les MRPs : nouveaux acteurs dans la migration leucocytaires. Centre de Recherche du CHUL, Quebec city, Canada. 2 April 1998
12. Les MRPs et la réaction inflammatoire. INRS-Santé, Montreal, Canada. 12 March 1998
13. Chemokine gene expression in a murine model of leukocyte recruitment to extravascular sites. Medicity, University of Turku, Finland. 12 July 1996.
14. Chemokine gene expression in a murine model of leukocyte recruitment to extravascular sites. The Imperial Cancer Research Fund, London, U.K. 10 July 1996.
15. Chemokine gene expression in a murine model of leukocyte recruitment to extravascular sites. William Harvey Research Institute, London, U.K. 9 July 1996.

## ABSTRACTS

1. M.-A. Raquil, N. Anceriz, P.A. Tessier. S100A8 and S100A9 induce the proliferation of acute and chronic myeloid leukemia cells. Making Connections (NCIC meeting), Toronto, Canada, November 2007.
2. N. Anceriz, C. Gilbert, P.A. Tessier. S100A9 enhances neutrophil migration across endothelial cells. 2007 Canadian Arthritis Network Annual Scientific Conference, Halifax, Canada, October 2007.
3. M.-A. Raquil, C. Gilbert, P.A. Tessier. The chemotactic proteins S100A8 and S100A9 induce the proliferation of myeloid progenitor cells: possible role in rheumatoid arthritis. 2007 Canadian Arthritis Network Annual Scientific Conference, Halifax, Canada, October 2007.

4. N. Anceriz, C. Gilbert, P.A. Tessier. La S100A9 augmente la migration transendothéliale des neutrophiles. 49<sup>th</sup> Congrès du Club de Recherche Clinique du Québec, Lac-à-l'Eau-Claire, Canada, September 2007.
5. N. Anceriz, C. Gilbert, P.A. Tessier. S100A9 enhances neutrophil migration across human umbilical vein endothelial cells. 13<sup>th</sup> International Congress of Immunology, Rio de Janeiro, Brazil, August 2007.
6. M.-A. Raquil, K. Vandal, P. Rouleau, F. Barabé, C. Gilbert, P.A. Tessier. S100A8 and S100A9 proteins induce the proliferation of myeloid leukemia cells. 13<sup>th</sup> International Congress of Immunology, Rio de Janeiro, Brazil, August 2007.
7. 48<sup>th</sup> Congrès du Club de Recherche Clinique du Québec, Lac-à-l'Eau-Claire, Canada, September 2006. M.-A. Raquil, N. Anceriz, P.A. Tessier. Les protéines S100 et la migration des leucocytes au site infectieux. 48<sup>th</sup> Congrès du Club de Recherche Clinique du Québec, Lac-à-l'Eau-Claire, Canada, September 2006.
8. M.-A. Raquil, K. Vandal, P. Rouleau, P.A. Tessier. S100A8, S100A9, and S100A12 stimulate the proliferation of hematopoietic cells. 12<sup>th</sup> International Congress of Immunology and 4<sup>th</sup> Annual Conference of FOCIS, Montreal, Canada, July 2004.
9. N. Anceriz, K. Vandal, P.A. Tessier. Different effects of S100A8, S100A9, and S100A12 on neutrophil adhesion to endothelial cells and extracellular matrix proteins. 12<sup>th</sup> International Congress of Immunology and 4<sup>th</sup> Annual Conference of FOCIS, Montreal, Canada, July 2004.
10. J. Denis, P. Rouleau, K. Vandal, P.A. Tessier, D. Leclerc. The plant potexvirus Papaya Mosaic Virus triggers a strong immune response in mouse. 12<sup>th</sup> International Congress of Immunology and 4<sup>th</sup> Annual Conference of FOCIS, Montreal, Canada, July 2004.
11. K. Vandal, C. Ryckman, P. Rouleau, P.A. Tessier. The chemotactic factors S100A8 and S100A9 are involved in neutrophil release from bone marrow and migration to the inflammatory site in response to LPS. 17<sup>th</sup> Annual Spring Meeting of the Canadian Society for Immunology, Lake Louise, Canada, March 2003.
12. C. Ryckman, R. Cantin, G. Robichaud, M.J. Tremblay, P.A. Tessier. The pro-inflammatory Myeloid Related Proteins activate HIV replication in infected T-lymphocytes. 9<sup>th</sup> Conference on retroviruses and opportunistic infections. Seattle, USA, February 2002.
13. C. Ryckman, K. Vandal, P. Rouleau, M. Talbot, P.A. Tessier. Myeloid related proteins are associated with neutrophil accumulation induced by monosodium urate crystals. Stockholm, Sweden, July 2001.
14. C.J. Roberge, M. Gauthier, V. Lavaste, P.A. Tessier, D. Girard. Activation of human neutrophils *in vitro* and induction of neutrophilic inflammation *in vivo* by toxaphene. Canadian Society of Immunology 15<sup>th</sup> Annual Meeting, Lake Louise, Canada, April 2001.
15. M. Gauthier, C.J. Roberge, P.A. Tessier, D. Girard. Propriétés pro-inflammatoires du toxaphène *in vivo* et *in vitro*. Colloque annuel du Centre de recherche en toxicologie de l'environnement (TOXEN), Montréal, Canada, December 2000.
16. M. Pelletier, P.A. Tessier, D. Girard. Activation des neutrophiles *in vitro* et induction d'une inflammation neutrophilique *in vivo* par le dieldrine. Colloque annuel du Centre de recherche en toxicologie de l'environnement (TOXEN), Montréal, Canada December 2000.
17. P.A. Tessier. Les Myeloid Related Proteins et la réponse inflammatoire, 68<sup>e</sup> congrès de l'Association Canadienne-Française pour l'Avancement des Sciences, Montréal, Canada, May 2000
18. C. Ryckman, K. Vandal, P.A. Tessier. Sécrétion des protéines MRP (Myeloid Related

- Proteins) par les neutrophiles activés avec les cristaux d'urate monosodique (MSU). 68<sup>e</sup> congrès de l'Association Canadienne-Française pour l'Avancement des Sciences, Montréal, Canada, May 2000
19. C. Ryckman, K. Vandal P.A. Tessier. Secretion of myeloid related proteins (MRP) by monosodium urate crystal-stimulated neutrophils. Canadian Society of Immunology. Bromont, Canada, March 2000.
  20. R.D. May, P.A. Tessier, M.J. Robinson, N. Hogg. A functional investigation of the murine S100 protein MRP-14, *in vitro* and *in vivo*. Inflammation Paris 99, Paris, France, June 1999.
  21. R.D. May, P.A. Tessier, M.J. Robinson, N. Hogg. A functional investigation of the murine S100 protein MRP-14, *in vitro* and *in vivo*. Workshop on neutrophil development and functions. Madrid, Spain, April 1999.
  22. R. May, P.A. Tessier, M. J. Robinson, N. Hogg. Expression of murine MRP-14: *in vitro* and *in vivo* functions. Imperial Cancer Research Fund Annual Colloquium, Warwick, U.K., April 1998.
  23. N. Hogg, A. McDowall, P.A. Tessier, R. Newton. Regulation of  $\beta_2$  integrin function. Keystone meeting on leukocyte-endothelium adhesion. Lake Tahoe, Colorado, U.S.A., March 1998.
  24. P.A. Tessier, P.A. Hessian, R. Poulson, N. Hogg. Myeloid cells releases MRP proteins onto endothelium. 12<sup>th</sup> Spring meeting of the Canadian Society for Immunology, Sainte-Adèle, Canada, March 1998.
  25. P.A. Tessier<sup>1</sup>, P.H. Naccache, K. Neote, S.R. McColl. Induction by TNF $\alpha$  of chemokine gene expression in a murine model of leukocyte recruitment to extravascular sites. 10<sup>th</sup> Spring meeting of the Canadian Society for Immunology, Sainte-Adèle, Canada, March 1996.
  26. P.A. Tessier, P.H. Naccache, K. Neote, S.R. McColl. Chemokine gene expression in a murine model of leukocyte recruitment to extravascular sites. Chemotactic cytokines: Targets for novel therapeutic development, Philadelphia, Pennsylvania, U.S.A., October 1995.
  27. P. Tessier, S.R. McColl. Involvement of both ICAM-1 and VCAM-1 in the adhesion of monocytes and lymphocytes to synovial fibroblasts. Joint Meeting of the American Association of Immunologists and the Clinical Immunology Society, Denver, Colorado, U.S.A., May 1993.
  28. P. Tessier<sup>1</sup>, M. Audette, S.R. McColl. Regulation by tumor necrosis factor  $\alpha$  of intercellular adhesion molecule-1 gene expression in human synovial fibroblasts. Annual Meeting of the Royal College of Physicians and Surgeons of Canada, Quebec city, Canada, September 1991.
  29. P. Tessier, M. Audette, S.R. McColl. Regulation by tumor necrosis factor  $\alpha$  of intercellular adhesion molecule-1 gene expression in human synoviocytes. Federation of American Societies for Experimental Biology, Atlanta, U.S.A., April 1991.
  30. M. Audette, M. Bouillon, P. Tessier. Stimulated expression of intercellular adhesion molecule-1 (ICAM-1) by retinoic acid on human tumor cell lines. Karger Symposium "Cell to Cell Interaction", Basel, Switzerland, August 1990.
  31. M. Bouillon, N. Liao, P. Tessier, M. Audette. Expression de la ICAM-1 sur des lignées de tétocarcinomes humains et régulation de son expression par l'acide rétinoïque. Association Canadienne-Française pour l'Avancement des Sciences, 58<sup>ème</sup> Congrès, Quebec city, Canada, May 1990.

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<sup>1</sup>Selected for oral presentation in a workshop.

## OTHER ACTIVITIES

## COMMITTEE MEMBERSHIP

### Peer review committees

- 2005-2007 Member, Strategic Training Program Grant Mid-Term Committee, CIHR  
2001-2002 Member, Immunology Committee, Arthritis Society grant program  
2000 Invitee, Immunology Committee, Arthritis Society grant program

### Meetings

- 2006 Chairman, Colloque sur l'inflammation et l'apoptose, 48<sup>th</sup> meeting of the Club de Recherches cliniques du Québec, Lac-à-l'Eau-Claire, Canada, September 2006  
2006 Chairman, Workshop on Inflammation and Transplantation, Canadian Society for Immunology 19th Annual meeting, Halifax, June 2006  
2003 Organiser, Microbiology, Virology and Immunology section, 71<sup>st</sup> ACFAS meeting, Rimouski, May 2003  
2002-2004 Organiser, Social activities, 12<sup>th</sup> International Congress of Immunology, Montreal, July 2004  
2002 Organiser, Microbiology, Virology and Immunology section, 70<sup>th</sup> ACFAS meeting, Quebec City, May 2002

## REVIEWER

Associate editor, *Journal of Immunology* (2007-present)

### Reviewer

*Acta Paediatrica*  
*American Journal of Respiratory Care Critical Medicine*  
*Arthritis Research & Therapy*  
*European Pharmacology*  
*FASEB Journal*  
*International Immunopharmacology*  
*Journal of Biological Chemistry*  
*Journal of Immunology*  
*Journal of Investigative Dermatology*  
*Journal of Leukocyte Biology*  
*Journal of Parasitology*  
*Neurobiology of Aging*

## SUPERVISORY EXPERIENCE

1. Julie Andrea Chapeton, Ph.D. Microbiology-Immunology, Faculty of Medicine, Université Laval, 2008-present.
2. Jean-Christophe Simon, M.Sc. (co-supervisor), Microbiology-Immunology, Faculty of Medicine, Université Laval, 2008-present

3. Alain Boulende, M.Sc. (co-supervisor), Microbiology-Immunology, Faculty of Medicine, Université Laval, 2005-2006.
4. Jérôme Denis, Ph.D. (co-supervisor), Microbiology-Immunology, Faculty of Medicine, Université Laval, 2003-present.
5. Marie-Astrid Raquil, Ph.D., Microbiology-Immunology, Faculty of Medicine, Université Laval, 2003-present.
6. Nadia Anceriz, Ph.D., Microbiology-Immunology, Faculty of Medicine, Université Laval, 2003-present.
7. Pascal Rouleau, M.Sc., Microbiology-Immunology, Faculty of Medicine, Université Laval, 2002-2003.
8. Carle Ryckman, Ph.D., Microbiology-Immunology, Faculty of Medicine, Université Laval, 1999-2004.

## **THESIS (REFeree)**

### **Ph.D.**

1. Jocelyn Roy  
Microbiology-Immunology, Faculty of medicine, Université Laval, 5 July 2007  
Examinator
2. Carle Ryckman  
Microbiology-Immunology, Faculty of medicine, Université Laval, 25 February 2004  
Supervisor
3. Claudine Matte  
Microbiology-Immunology, Faculty of medicine, Université Laval, 15 February 2000  
Examinator

### **M.Sc.**

1. Marie-Christine Dumas  
Microbiology-Immunology, Faculty of medicine, Université Laval, 9 May 2007  
Examinator
2. Marie-Ève Champagne  
Microbiology-Immunology, Faculty of medicine, Université Laval, 1 May 2007  
Examinator
3. Catherine Matron  
Microbiology-Immunology, Faculty of medicine, Université Laval, 20 February 2007  
Examinator
4. Alain Boulende  
Microbiology-Immunology, Faculty of medicine, Université Laval, 20 October 2006  
Co-supervisor
5. Jean-François Gauthier  
Microbiology-Immunology, Faculty of medicine, Université Laval, 4 October 2006  
Examinator
6. Caroline Bélanger  
Pharmacie, Faculté de pharmacie, Université de Montréal, 22 August 2006

- Examinator
7. Valérie Garceau  
Microbiology-Immunology, Faculty of medicine, Université Laval, 15 September 2003  
Examinator
  8. Claude Ratthé  
INRS-IAF/Santé humaine, 3 June 2003  
Examinator
  9. Andrée Maheux  
Microbiology-Immunology, Faculty of medicine, Université Laval, 10 February 2003  
Examinator
  10. Pascal Rouleau  
Microbiology-Immunology, Faculty of medicine, Université Laval, 22 January 2003  
Supervisor
  11. Julie Nieminen  
Microbiology-Immunology, Faculty of medicine, Université Laval, 17 January 2003  
Examinator
  12. Geneviève Lachance  
Microbiology-Immunology, Faculty of medicine, Université Laval, 24 April 2002  
Examinator
  13. Marc Gauthier  
INRS-IAF/Santé humaine, 15 October 2001  
Examinator
  14. Valérie Lavastre  
INRS-IAF/Santé humaine, 17 September 2001  
Examinateur externe
  15. Frédéric Dallaire  
Microbiology-Immunology, Faculty of medicine, Université Laval, 14 February 2001  
Examinator
  16. Martin Pelletier  
INRS-IAF/Santé humaine, 29 September 2000  
Examinator
  17. Philippe Desaulniers  
Microbiology-Immunology, Faculty of medicine, Université Laval, 19 June 2000  
Examinator
  18. Isabelle Filion  
Microbiology-Immunology, Faculty of medicine, Université Laval, 20 October 1999  
Examinator

## **TEACHING**

### **Undergraduate (Total 37 hours)**

- 2008 Sciences Fondamentales (MCB-23243), 4 credits, 11 hours, collaborator  
2006-2007 Immunologie médicale (MCB-21551), 1 credit 15 hours, Coordinator  
2005-present Pharmacologie moléculaire (PHM2302, U. de Montréal), 3 credit, 2 hours  
Collaborator  
2004-present Immunologie médicale (MCB-17902), 1 credit, 20 hours  
Coordinator

### **Graduate (Total 78 hours)**

- 2003-present Séminaire I (MCB-62699), 1 credit, 30 hours  
Coordinator  
2003-present Séminaire II (MCB-64140), 1 credit, 30 hours  
Coordinator  
2003-present La réaction inflammatoire (MCB-63801), 3 crédits, 3 hours, Collaborator  
2003-present Cytokines, chimiokines et facteurs de croissance (PHM6034, U. de Montréal), 3  
credits, 6 hours, Collaborator  
2000-present Immunopathogénèse des maladies infectieuses (MCB-63803), 3 credits, 3 hours,  
Collaborator  
2000-present Immunologie cellulaire (MCB-63602), 3 credits, 3 hours, Collaborator

## RESEARCH INTERESTS

My laboratory is investigating the roles and mechanisms of action of S100A8, S100A9, and S100A12 in immune responses and leukemia. These proteins are collectively referred to as myeloid-related proteins and are now considered to be alarmins (intracellular proteins released during immune responses that activate the immune system). S100A8, S100A9, and S100A12 are small calcium-binding proteins expressed abundantly in the cytosol of neutrophils and at lower levels in monocytes, as well as by activated epithelial and endothelial cells. They exist as noncovalently bonded homodimers and form a noncovalent heterodimer called S100A8/A9 or calprotectin. Interestingly, massive levels of S100A8/A9 are observed in serum and at inflammatory sites of patients suffering from Crohn disease, ulcerative colitis, and rheumatoid arthritis, to name a few. They are also highly expressed in acute and chronic myeloid leukemia (AML and CML), and several solid tumor cancers.

### **S100A8, S100A9, and S100A12 in immune responses**

We have recently demonstrated that these proteins are chemotactic for neutrophils and are essential to neutrophil migration. We and others demonstrated that they are secreted via a nonclassical pathway dependent of tubulin polymerisation during neutrophil and monocyte interaction with the endothelium. In addition, we demonstrated that S100A8, S100A9, and S100A12 induce neutrophil adhesion to fibrinogen, fibronectin and endothelial cells, as well as their release from the bone marrow. More importantly, up to 80% of neutrophil and macrophage migration to the inflamed lung alveoli is abrogated by anti-S100A8 and anti-S100A9. Thus, they play a major role in leukocyte migration to the inflammatory site, but their exact mechanism of action remains largely unknown. We are currently investigating their mechanism of action by intravital microscopy.

We demonstrated that S100A8 and S100A9 stimulate NF $\kappa$ B in CD4<sup>+</sup> T lymphocytes. In collaboration with Dr Olivier from McGill University, we demonstrated that myeloid-related proteins induce NO production in murine macrophages via activation of the MEK/ERK cascade. Preliminary results also indicate that they induce dendritic cell maturation. In the next few years, we intend to investigate their effects on T and B lymphocyte activation, as well as dendritic cell maturation. We are also investigating their roles in rheumatoid arthritis and inflammatory bowel diseases using the mouse collagen-induced arthritis and the TNBS and oxazolone-induced colitis models respectively.

### **S100A8, S100A9, and S100A12 in normal and pathological haematopoiesis**

We also examined the effect of S100A8 and S100A9 on the proliferation of AML, CML, and K562 cells in vitro. We showed that S100A8 and S100A9 induce leukemia cell proliferation. A direct correlation between S100A8/A9 concentrations in AML and CML sera and the proliferation rate of K562 cells induced by AML and CML sera was observed. Furthermore, antibodies against S100A8 and S100A9 inhibit leukemia cell proliferation induced by AML and CML patient sera. These results indicate that S100A8 and S100A9 are autocrine growth factors in AML and CML. S100A8 and S100A9 also induce breast cancer cell proliferation, prostate cancer cell migration and promote metastasis to the lung. Preliminary results also suggest that S100A9 stimulates haematopoietic stem cell proliferation, as well as myelopoiesis. We are currently trying to identify the receptors for these new cytokines, as well as to decipher their signal transduction mechanism in leukemia cells.